REMARKS

Status of the Claims.

Claims 1-4, 7-9, 11-22, and 24-33 are pending with entry of this amendment, claims 5, 6, 10, and 23 being cancelled and no claims being added. Claims 1, 9, 21, and 22 are amended herein. These amendments introduce no new matter. Support is replete throughout the specification (*e.g.*, in the claims as originally filed).

Change in correspondence address.

Please direct all future correspondence regarding the subject application to CUSTOMER NUMBER 22798, that is:

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35 U.S.C. §112, Second Paragraph.

Claims 1-9, 11-22, and 24-33 were rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite because of the phrase "synergistic combination". The claims are amended herein to eliminate the term "synergistic combination" thereby obviating this rejection.

35 U.S.C. §103(a).

Claims 1-6, 9, 1-22, and 24-33 were rejected under 35 U.S.C. §103(a) as allegedly obvious in light of Yu *et al.* (U.S. Patent 5,385,938) in view of Poli *et al.* (1979) Food Chemistry, 443: 251-258, Wenninger (International Cosmetic Ingredient Dictionary and Handbook, 7th Ed., 1: 163-168, Merck Index 11th ed. (1989) Glycolic acid monograph 4394, page 439, and Pamukoff (Canadian Patent 1, 221,640). According to the Examiner, Yu *et al.* teaches a topical composition with glycolic acid as the active ingredient and ethanol as the solvent. Poli *et al.* is cited as allegedly teaching that glycolic acid is virucidal against herpesvirus. Wenninger is cited as allegedly teaching that butylenes

glycol is useful as a solvent in numerous cosmetic marketed products. The Merck index allegedly teaches that the pH of 0.5% glycolic acid solution is 2.50. Pamukoff allegedly teaching the use of 1-10% ethyl alcohol containing compositions for treating viral infections broadly. Applicants traverse.

The Examiner is respectfully reminded that *prima facie* case of obviousness requires that the combination of the cited art, taken with general knowledge in the field, must provide all of the elements of the claimed invention. When a rejection depends on a combination of prior art references, there must be some **teaching, suggestion, or motivation to combine** the references. *In re Geiger*, 815 2 USPQ2d 1276, 1278 (Fed. Cir. 1987). Moreover, to support an obviousness rejection, the cited references must additionally **provide a reasonable expectation of success**. *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991), *citing In re Dow Chemical Co.,* 5 USPQ2d 1529, 1531 (Fed. Cir. 1988).

In addition, the Examiner is also reminded that the MPEP expressly states that "**if the proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification**. MPEP §2143.01, *citing In re Gordon*, 221 USPQ 1125 (Fed. Cir. 1984).

In the instant case, modification of the compositions of Yu *et al.*would make the formulation unsatisfactory for Yu et al.'s intended purpose. Moreover, Yu *et al.* expressly teach away from the presently claimed formulation. In particular, Yu *et al.* teach the use of compositions containing **both**:

1) an **amphoteric or pseudoamphoteric** compound; and
2) **alpha hydroxyacids, alpha ketoacids** or related compound.

Thus, for example, Yu *et al.* expressly states:

> It has now been discovered that **amphoteric compositions** containing alpha hydroxyacids, alpha ketoacids or related compounds, and also the compositions containing dimeric or polymeric forms of hydroxyacids overcome the aforementioned shortcomings and retain the therapeutic efficacies for cosmetic conditions and dermatologic disorders. **The amphoteric composition contains in combination an amphoteric or pseudoamphoteric compound and at least one of the alpha hydroxyacids, alpha ketoacids or related compounds**. [emphasis added] (col. 3, lines 10-12).,

> The amphoteric composition of the instant invention contains in combination an **alpha hydroxyacid or alpha ketoacid and an amphoteric or pseudoamphoteric compound**. [emphasis added]

This is illustrated by Example 1 (col. 14, lines 1-10) which states:

> An amphoteric composition containing 1M **2-hydroxyethanoic acid and 0.5M L-arginine** in solution form for dandruff or dry skin may be formulated as follows.
> 2-Hydroxyethanoic acid (glycolic acid) 7.6 g is dissolved in water 60 ml and propylene glycol 20 ml. **L-Arginine 8.7 g is added to the solution** with stirring until all the crystals are dissolved. Ethanol is added to make a total volume of the solution to 100 ml. The amphoteric composition thus formulated has pH 3.0. An amphoteric composition formulated from 1M 2-hydroxyethanoic acid and 1M L-arginine has pH 6.3. **The solution has pH 1.9 if no amphoteric compound is incorporated.** [emphasis added]

In this instance, 2-hydroxyethanoic acid is the alphahydroxy acid, while **L-arginine is the amphoteric compound**. *See, e.g.,* col.5, lines 1-7 which state:

> The **representative amphoteric compounds of amino acid type may be listed as follows: Glycine**, alanine, valine, leucine, isoleucine, serine, threonine, cysteine, cystine, methionine, aspartic acid, asparagine, glutamic acid, glutamine, arginine, lysine, 5-hydroxylysine, histidine, phenylalanine, tyrosine, tryptophan, 3-hydroxyproline, 4-hydroxyproline and proline. [emphasis added]

Elimination of the L-arginine (the amphoteric compound) to produce a composition consisting of glycolic acid and ethanol as proposed by the Examiner (*see*, Office Action, page 4, lines 10-12) would defeat the central teaching of the Yu *et al.* patent. Moreover, Yu *et al.* expressly teaches that in the absence of the amphoteric compound, the solution has a pH of 1.9 which is lower than the pH of 2.45 to 4.5 recited in the pending claims.

Yu *et al.* thus, by teaching the necessity of an amphoteric or pseutoamphoteric compound, expressly leads one of skill away from the presently claimed invention. Moreover, elimination of the amphoteric compound would defeat the central teaching of Yu *et al.* and render their compounds unsuitable for the intended use.

Yu *et al.* thus fails to teach or suggest the presently claimed invention and expressly teaches away. The defects of Yu *et al.* are not remedied by Poli *et al.* Wenninger, the Merck Index, or Pamukoff.

For example, Poli *et al.* allegedly teaches that glycolic acid is virucidal against herpesvirus. Poli *et al.*, however, only evaluates the virucidal activity of organic acids when tested in culture against various strains. Poli *et al.* offers no teaching or suggestion of the combination of glycolic aicd and an alcohol as presently claimed. Poli *et al.* offers no teaching or suggestion that such a combination would synergistically enhance the virucidal activity of the acid as recited in the presently pending claims. Moreover, the Merck index, cited by the Examiner expressly states:

> Use: In the processing of textiles, leather, and metals; in pH control, and wherever a cheap organic acid is needed, *e.g.,* in the manuf of adhesives, in copper brightening, decontamination cleaning, dyeing, electroplating, in pickling, cleaning and chemical milling of metals. ***Caution:*** **Mild irritant to skin, mucous membranes.**

By teaching that glycolic acid is an irritant, the Merck index leads one of skill away from the use of glycolic acid in topical applications. The combination of Yu *et al.*, Poli *et al.*, and/or the Merck Index, simply offers no teaching or suggestion of the presently claimed invention and, in fact teaches away from such an invention.

The defects of these references are not remedied by Wenninger or Pamukoff.

Pamukoff teaches pharmaceutical compositions comprising glycerine, ethyl alcohol, **and an alkali metal halide salt**:

> Thus according to one aspect of the present invention, there is provided a pharmaceutical composition for use in topical application to alleviate virus infections of the herpes family of viruses and common cold virus, which comprises from about **2.5 to 5.0 parts, by weight of glycerine**, from about 1 to about 10 parts by weight of ethyl alcohol, and from 0 to about 1 part by weight of a physicologically acceptable **alkali metal halide** salt. [emphasis added (page 2, paragraph 2)
>
> * * *
>
> Preferably such formulations are proivded ina prameceucailly acceptable carrier base. . . . a suitalb eamount of water for use with the aobvbe-

formualtion being from about 80 to about 120 parts by wieght. (page 2, 3rd paragraph).

Thus, **Pamukoff teaches the necessity of a halide salt**. Moreover, as indicated above, both the glycerine and the halide salt are regarded as active ingredients, not a pharmaceutically acceptable carrier base. By teaching the requirement of a halide salt and by offering no teaching or suggestion of the presently claimed combination of alcohol and acid, Parmukoff expressly leads one of skill away from the presently claimed invention.

Wenninger teaches that butylenes glycol is found in a number of skin care products. Wenninger further teaches that butylene glycol is a viscosity increasing agent. Wenninger offers no teaching or suggestion that butylenes glycol functions is useful in a virucidal composition.

The cited references alone, or in combination thus fail to teach or suggest the presently claimed invention. Moreover, by teaching the **necessary inclusion of an amphoteric or pseudoamphoteric** compound (Yu *et al.*), by teaching that glycolic acid is an **irritant of skin** and mucous membranes (Merck Manual), by teaching the **necessity of a halide salt** (Pamukoff), the combination of references expressly lead one of skill away from the presently claimed method. Accordingly the Examiner has failed to make his *prima facie* case and the rejection of claims 1-6, 9, 1-22, and 24-33 under 35 U.S.C. §103(a) should be withdrawn.

In view of the foregoing, Applicants believes all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested. **Should the Examiner seek to maintain the rejections, Applicants request a telephone interview with the Examiner and the Examiner's supervisor.**

If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (510) 769-3513.

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Respectfully submitted,

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